FILE 'MEDLINE, USPATFULL, WPIDS, BIOSIS, EMBASE, CAPLUS' ENTERED AT 19:07:37 ON 14 MAY 2004

L1 103537 S ANGIOGENESIS OR ANTI-ANGIOGENESIS
L2 885063 S OCCULAR OR EYE
L3 3276303 S CANCER OR NEOPLASM
L4 4114364 S L2 OR L3
L5 50134 S L4 AND L1
L6 87 S NEPAFENAC
L7 17 S L6 AND L5
L8 10297 S COX-2 INHIBITOR
L9 944 S L8 AND L5
L10 724 DUPLICATE REMOVE L9 (220 DUPLICATES REMOVED)
L11 48 S L10 AND PY<=1999

=> d 1-48 bib abs

L11 ANSWER 1 OF 48 MEDLINE on STN
AN 2000393805 MEDLINE
DN PubMed ID: 10919714
TI Upregulation of vascular endothelial growth factor by cobalt chloride-simulated hypoxia is mediated by persistent induction of cyclooxygenase-2 in a metastatic human prostate **cancer** cell line.
AU Liu X H; Kirschenbaum A; Yao S; Stearns M E; Holland J F; Claffey K; Levine A C
CS Department of Medicine, Mount Sinai School of Medicine, New York, NY 10029, USA.. liux01@doc.mssm.edu
SO Clinical & experimental metastasis, **(1999)** 17 (8) 687-94.
Journal code: 8409970. ISSN: 0262-0898.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000824
Last Updated on STN: 20021219
Entered Medline: 20000817
AB Upregulation of vascular endothelial growth factor (VEGF) expression induced by hypoxia is crucial event leading to neovascularization. Cyclooxygenase-2, an inducible enzyme that catalyzes the formation of prostaglandins (PGs) from arachidonic acid, has been demonstrated to be induced by hypoxia and play role in **angiogenesis** and metastasis. To investigate the potential effect of COX-2 on hypoxia-induced VEGF expression in prostate **cancer**. We examined the relationship between COX-2 expression and VEGF induction in response to cobalt chloride (CoCl2)-simulated hypoxia in three human prostate **cancer** cell lines with differing biological phenotypes. Northern blotting and ELISA revealed that all three tested cell lines constitutively expressed VEGF mRNA, and secreted VEGF protein to different degrees (LNCaP > PC-3 > PC3ML). However, these cell lines differed in the ability to produce VEGF in the presence of CoCl2-simulated hypoxia. CoCl2 treatment resulted in 40% and 75% increases in VEGF mRNA, and 50% and 95% in protein secretion by LNCaP and PC-3 cell lines, respectively. In contrast, PC-3ML cell line, a PC-3 subline with highly invasive, metastatic phenotype, exhibits a dramatic upregulation of VEGF, 5.6-fold in mRNA and 6.3-fold in protein secretion after treatment with CoCl2. The upregulation of VEGF in PC-3ML cells is accompanied by a persistent induction of COX-2 mRNA (6.5-fold) and protein (5-fold). Whereas COX-2 expression is only transiently induced in PC-3 cells and not affected by CoCl2 in LNCaP cells. Moreover, the increases in VEGF mRNA and protein secretion induced by CoCl2 in PC-3ML cells were significantly suppressed following exposure to NS398, a selective **COX-2 inhibitor**. Finally, the effect of COX-2 inhibition on CoCl2-induced VEGF production was reversed

by the treatment with exogenous PGE2. Our data demonstrate that VEGF induction by cobalt chloride-simulated hypoxia is maintained by a concomitant, persistent induction of COX-2 expression and sustained elevation of PGE2 synthesis in a human metastatic prostate **cancer** cell line, and suggest that COX-2 activity, reflected by PGE2 production, is involved in hypoxia-induced VEGF expression, and thus, modulates prostatic tumor **angiogenesis**.

L11 ANSWER 2 OF 48 MEDLINE on STN
AN 2000133664 MEDLINE
DN PubMed ID: 10668485
TI **COX-2 inhibitors**. A new class of antiangiogenic agents.
AU Masferrer J L; Koki A; Seibert K
CS Discovery Pharmacology and Analytical Sciences Center, G.D. Searle/Monsanto Company, St. Louis, Missouri 63167, USA.. jlmasf@monsanto.com
SO Annals of the New York Academy of Sciences, **(1999)** 889 84-6.
Ref: 7
Journal code: 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302
AB The formation of new blood vessels by **angiogenesis** to provide adequate blood supply is a key requirement for the growth of many tumors. While normal blood vessels expressed the COX-1 enzyme, new angiogenic endothelial cells expressed the inducible COX-2. We evaluated the role of COX inhibitors in the mouse corneal micropocket assay in which **angiogenesis** is driven by the addition of a Hydron pellet containing basic fibroblast growth factor (bFGF). Neovascular areas were measured with a slit lamp five days after pellet implantation into the corneal stroma. All animals containing implants with bFGF (90 ng) developed intensive areas of neovascularization, whereas the controls implanted with the Hydron pellet alone did not. Indomethacin (a nonselective COX-1/**COX-2 inhibitor**) and SC-236 (a COX-2-selective inhibitor) inhibited **angiogenesis** in a dose-dependent manner. Importantly, the indomethacin-treated mice developed severe gastrointestinal toxicity at the efficacious dose of 3 mg/kg/day. By contrast, gastrointestinal lesions were not observed, and platelet COX-1 activity was unaffected, at anti-angiogenic doses of SC-236 (1-6 mg/kg/day). Furthermore, a COX-1-selective inhibitor, SC-560, was ineffective at doses up to 10 mg/kg, a dose that completely blocked platelet COX-1 activity in these mice. SC-236 was also effective in reducing **angiogenesis** driven by bFGF, vascular endothelium growth factor (VEGF), or carrageenan in the matrigel rat model. Finally, in several tumor models, SC-236 consistently and effectively inhibited tumor growth and **angiogenesis**. This novel antiangiogenic activity of **COX-2 inhibitors** indicates their potential therapeutic utility in several types of **cancer**.

L11 ANSWER 3 OF 48 MEDLINE on STN
AN 2000081944 MEDLINE
DN PubMed ID: 10616198
TI Cyclooxygenase inhibitors suppress **angiogenesis** and reduce tumor growth in vivo.
AU Sawaoka H; Tsuji S; Tsujii M; Gunawan E S; Sasaki Y; Kawano S; Hori M
CS Department of Internal Medicine and Therapeutics, Oska University Graduate

School of Medicine, Suita, Japan.
SO Laboratory investigation; a journal of technical methods and pathology, **(1999 Dec)** 79 (12) 1469-77.
Journal code: 0376617. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000124
Last Updated on STN: 20021219
Entered Medline: 20000113
AB **Angiogenesis** plays a key role in the development of malignant tumors. To clarify the roles of cyclooxygenase (COX) in malignant tumor development and **angiogenesis**, we investigated the effects of COX inhibitors on two kinds of gastrointestinal **cancer** xenograft, one of which overexpresses COX-2 and the other expresses no COX, in nude mice in vivo. There was a positive correlation between tumor volume and **angiogenesis** within the xenograft. Oral administration with a specific COX-2 or a nonspecific COX inhibitors lowered the expression of potent angiogenic factors; vascular endothelial growth factor and basic fibroblast growth factor, reduced **angiogenesis** and growth, induced apoptosis, and suppressed cell replication of the COX-2 overexpressing **cancer** xenografts in a dose-dependent manner. A nonspecific COX inhibitor, not a specific **COX-2 inhibitor**, reduced growth and **angiogenesis** of non-COX expressing **cancer** xenograft by inhibition of COX-1 in vascular endothelial cells. These results demonstrate that COX inhibitors suppress **angiogenesis** and tumor growth by inhibiting expression of angiogenic factors and vascular endothelial cell growth. They support the hypothesis that COX plays an important role in **cancer** growth via **angiogenesis**. These findings offer a new strategy against **cancer** using COX inhibitors (nonsteroidal anti-inflammatory drugs).

L11 ANSWER 4 OF 48 MEDLINE on STN
AN 2000061194 MEDLINE
DN PubMed ID: 10595745
TI A selective cyclooxygenase-2 inhibitor suppresses tumor growth in nude mouse xenografted with human head and neck squamous carcinoma cells.
AU Nishimura G; Yanoma S; Mizuno H; Kawakami K; Tsukuda M
CS Department of Otorhinolaryngology, Yokohama City University School of Medicine.. go_c@med.yokohama-cu.ac.jp
SO Japanese journal of cancer research : Gann, **(1999 Oct)** 90 (10) 1152-62.
Journal code: 8509412. ISSN: 0910-5050.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000104
AB The anti-tumor effect of a selective cyclooxygenase (**COX**)-**2 inhibitor**, JTE-522, was examined with the human head and neck squamous cell carcinoma cell line KB. KB cells do not produce prostaglandin (PG)-E2. In vitro, JTE-522 induced an increase of G1 phase-arrested cells, suppression of platelet-derived growth factor (PDGF) production and inhibition of telomerase activity. No cytotoxic effect was detected. In vivo, the growth of the tumor xenografted into nude mice was significantly suppressed by JTE-522. Suppression of **angiogenesis** at the periphery of the tumor, increase of G1-arrested cells and suppression of telomerase activity were observed, together with an

increase of apoptotic cell death in the tumor. Immunological enhancement did not play a role. We concluded that the anti-tumor effect of JTE-522 was caused by **anti-angiogenesis** action, cell cycle arrest and inhibition of telomerase activity of the tumor cells. These combined effects might induce apoptosis.

L11 ANSWER 5 OF 48 MEDLINE on STN
AN 2000048163 MEDLINE
DN PubMed ID: 10581086
TI Inhibition of **angiogenesis** by nonsteroidal anti-inflammatory drugs: insight into mechanisms and implications for **cancer** growth and ulcer healing.
CM Comment in: Nat Med. 1999 Dec;5(12):1348-9. PubMed ID: 10581068
AU Jones M K; Wang H; Peskar B M; Levin E; Itani R M; Sarfeh I J; Tarnawski A S
CS Department of Medicine, Veterans Affairs Medical Center, 5901 East Seventh Street, Long Beach, California 90822, USA.
SO Nature medicine, **(1999 Dec)** 5 (12) 1418-23.
Journal code: 9502015. ISSN: 1078-8956.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20021219
Entered Medline: 19991229
AB **Angiogenesis**, the formation of new capillary blood vessels, is essential not only for the growth and metastasis of solid tumors, but also for wound and ulcer healing, because without the restoration of blood flow, oxygen and nutrients cannot be delivered to the healing site. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, indomethacin and ibuprofen are the most widely used drugs for pain, arthritis, cardiovascular diseases and, more recently, the prevention of colon **cancer** and Alzheimer disease. However, NSAIDs produce gastroduodenal ulcers in about 25% of users (often with bleeding and/or perforations) and delay ulcer healing, presumably by blocking prostaglandin synthesis from cyclooxygenase (COX)-1 and COX-2 (reference 10). The hypothesis that the gastrointestinal side effects of NSAIDs result from inhibition of COX-1, but not COX-2 (reference 11), prompted the development of NSAIDs that selectively inhibit only COX-2 (such as celecoxib and rofecoxib). Our study demonstrates that both selective and nonselective NSAIDs inhibit **angiogenesis** through direct effects on endothelial cells. We also show that this action involves inhibition of mitogen-activated protein (MAP) kinase (ERK2) activity, interference with ERK nuclear translocation, is independent of protein kinase C and has prostaglandin-dependent and prostaglandin-independent components. Finally, we show that both COX-1 and COX-2 are important for the regulation of **angiogenesis**. These findings challenge the premise that selective **COX-2 inhibitors** will not affect the gastrointestinal tract and ulcer/wound healing.

L11 ANSWER 6 OF 48 MEDLINE on STN
AN 1998292170 MEDLINE
DN PubMed ID: 9630216
TI Cyclooxygenase regulates **angiogenesis** induced by colon **cancer** cells.
CM Erratum in: Cell 1998 Jul 24;94(2):following 271
AU Tsujii M; Kawano S; Tsuji S; Sawaoka H; Hori M; DuBois R N
CS Department of Medicine, Vanderbilt University Medical Center, VA Medical Center, Nashville, Tennessee 37232, USA.
NC DK-47297 (NIDDK)
NIEHS-00267 (NCEH)
SO Cell, **(1998 May 29)** 93 (5) 705-16.

Journal code: 0413066. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X04677
EM 199807
ED Entered STN: 19980716
Last Updated on STN: 19990129
Entered Medline: 19980706
AB To explore the role of cyclooxygenase (COX) in endothelial cell migration and **angiogenesis**, we have used two in vitro model systems involving coculture of endothelial cells with colon carcinoma cells. COX-2-overexpressing cells produce prostaglandins, proangiogenic factors, and stimulate both endothelial migration and tube formation, while control cells have little activity. The effect is inhibited by antibodies to combinations of angiogenic factors, by NS-398 (a selective **COX-2 inhibitor**), and by aspirin. NS-398 does not inhibit production of angiogenic factors or **angiogenesis** induced by COX-2-negative cells. Treatment of endothelial cells with aspirin or a COX-1 antisense oligonucleotide inhibits COX-1 activity/expression and suppresses tube formation. Cyclooxygenase regulates colon carcinoma-induced **angiogenesis** by two mechanisms: COX-2 can modulate production of angiogenic factors by colon **cancer** cells, while COX-1 regulates **angiogenesis** in endothelial cells.

L11 ANSWER 7 OF 48 MEDLINE on STN
AN 1998221936 MEDLINE
DN PubMed ID: 9561165
TI Apoptosis induction and inhibition of colon-26 tumour growth and **angiogenesis**: findings on COX-1 and **COX-2 inhibitors** in vitro & in vivo and topical diclofenac in hyaluronan.
AU Seed M P; Freemantle C N; Alam C A; Colville-Nash P R; Brown J R; Papworth J L; Somerville K W; Willoughby D A
CS Royal London School of Medicine and Dentistry, United Kingdom.
SO Advances in experimental medicine and biology, **(1997)** 433 339-42.
Journal code: 0121103. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980618
Last Updated on STN: 20000303
Entered Medline: 19980611

L11 ANSWER 8 OF 48 USPATFULL on STN
AN 2003:228333 USPATFULL
TI Aryloxy substituted pyrimidine imidazole compounds
IN Adams, Jerry L., Wayne, PA, United States
Lee, Dennis, Foster City, CA, United States
Long, Scott A., Ballwin, MO, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6610695 B1 20030826
WO 9857966 19981223 <--
AI US 2000-445652 20000322 (9)
WO 1998-US12828 19980619
PRAI US 1997-50224P 19970619 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.

LREP Dinner, Dara L., Furman, Theodore R., Kinzig, Charles M.
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2009
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel 2,4,5-triaryl substituted imidazole compounds and compositions for use in therapy of CSBP/RK/p38 mediated diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 9 OF 48 USPATFULL on STN
AN 2003:222110 USPATFULL
TI 2,3-substituted indole compounds as anti-inflammatory and analgesic agents
IN Nakao, Kazunari, 29-1, Sinbayashi, Shinbayahi-cho, Chiryu-shi, Aichi-ken, JAPAN 472-0017
Stevens, Rodney William, 3-4-26, Seoshiro-cho, Handa-shi, Aichi-ken, JAPAN 484-0081
Kawamura, Kiyoshi, 40-1, Daimonsaki, Inuyama, Inuyama-shi, Aichi-ken, JAPAN 484-0081
Uchida, Chikara, 118-401, Miyaji-cho, Handa-shi, Aichi-ken, JAPAN 475-0902
Koike, Hiroki, 1-100 Souga-cho, Handa-shi, Aichi-ken, JAPAN 475-0801
Caron, Stephane, 600 Meridian St. Extension-Apt. 509, Groton, CT, United States 06340
PI US 6608070 B1 20030819
WO 9935130 19990715 <--
AI US 1999-355494 19990728 (9)
WO 1998-IB2065 19981218
DT Utility
FS GRANTED
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Richardson, Peter C., Ginsburg, Paul H., Catania, Richard L.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 10227
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a compound of the following formula: ##STR1##

or the pharmaceutically acceptable salts thereof wherein Z is OH, C1-6 alkoxy, --NR2R3 or heterocycle; Q is selected from the following: (a) an optionally substituted phenyl, (b) an optionally substituted 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), (c) an optionally substituted 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, (d) an optionally substituted C3-7 cycloalkyl and (e) an optionally substituted benzo-fuzed heterocycle; R1 is hydrogen, C1-4 alkyl or halo; R2 and R3 are independently hydrogen, OH, C1-4 alkoxy, C1-4 alkyl or C1-4 alkyl substituted with halo, OH, C1-4 alkoxy or CN; X is independently selected from H, halo, C1-4 alkyl, halo-substituted C1-4 alkyl, OH, C1-4 alkoxy, halo-substituted C1-4 alkoxy, C1-4 alkylthio, NO2, NH2, di-(C1-4 alkyl)amino and CN; and n is 0, 1, 2, 3 and 4.

This invention also provides a pharmaceutical composition useful for the treatment of a medical condition in which prostaglandins are implicated as pathogens.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 10 OF 48 USPATFULL on STN

AN 2003:143068 USPATFULL
TI Substituted imidazole compounds
IN Adams, Jerry L, Wayne, PA, United States
Hall, Ralph F, Villanova, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6569871 B1 20030527
WO 9901136 19990114 <--
AI US 1999-445860 19991215 (9)
WO 1998-US13808 19980701
PRAI US 1997-51584P 19970702 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Balasubramanian, Venkataraman
LREP Dinner, Dara L., Venetianer, Stephen, Kinzig, Charles M.
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2783
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel 1,4,5 substituted imidazole compounds and compositions for use in therapy as CSBP/p38 kinase inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 11 OF 48 USPATFULL on STN
AN 2003:129944 USPATFULL
TI Substituted imidazole compounds
IN Adams, Jerry L., Wayne, PA, United States
Boehm, Jeffrey C., King of Prussia, PA, United States
Gallagher, Timothy Francis, Harleysville, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6562832 B1 20030513
WO 9901131 19990114 <--
AI US 1999-446036 19991215 (9)
WO 1998-US13805 19980701
PRAI US 1997-51592P 19970702 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker B.
LREP Dinner, Dara L., Venetianer, Stephen, Kinzig, Charles M.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3605
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel 1,4,5-subsituted imidazole compounds and compositions for use in therapy as cytokine inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 12 OF 48 USPATFULL on STN
AN 2002:317428 USPATFULL
TI Substituted imidazole compounds
IN Adams, Jerry L., Wayne, PA, United States
Hall, Ralph F., Villanova, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6489325 B1 20021203
WO 9901130 19990114 <--
AI US 2000-446147 20000330 (9)

WO 1998-US13809 19980701
PRAI US 1998-51592P 19980701 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Liu, Hong
LREP Dinner, Dara L., Venetianer, Stephen, Kinzig, Charles M.
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2602
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel 1,4,5-substituted imidazole compounds and compositions for use in therapy as CSBP/p38 inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 13 OF 48 USPATFULL on STN
AN 2002:63911 USPATFULL
TI Cycloalkenyl substituted compounds
IN Adams, Jerry L., Wayne, PA, United States
Garigipati, Ravi, South Glastonbury, CT, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6362193 B1 20020326
WO 9917776 19990415 <--
AI US 2000-529214 20000407 (9)
WO 1998-US21189 19981008
20000407 PCT 371 date
PRAI US 1997-61351P 19971008 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Berch, Mark L.; Assistant Examiner: Habte, Kahsay
LREP Dinner, Dara L., Venetianer, Stephen, Kinzig, Charles M.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1523
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel pyridyl or pyrimidinyl substituted cycloalkenyl compounds and compositions for use in therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 14 OF 48 USPATFULL on STN
AN 2001:173617 USPATFULL
TI Indole compounds as **COX-2 inhibitors**
IN Stevens, Rodney William, Chita-gun, Japan
Nakao, Kasumari, Chita-gun, Japan
Kawamura, Kiyoshi, Chita-gun, Japan
Uchida, Chikara, Chita-gun, Japan
Fujiwara, Shinya, Chita-gun, Japan
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 6300363 B1 20011009
WO 9905104 19990204
AI US 1999-424837 19991203 (9)
WO 1998-IB1026 19980703
19991203 PCT 371 date
19991203 PCT 102(e) date
PRAI WO 1997-IB917 19970723
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Patel, Slidhaker B.
LREP Richardson, Peter C., Benson, Gregg C., Goddard, Carl J.

CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6541
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a compound of the following formula: ##STR1##

and the pharmaceutically acceptable salts thereof, wherein L is oxygen or sulfur; Y is a direct bond or C.sub.1-4 alkylidene; Q is C.sub.1-6 alkyl, C.sub.3-7 cycloalkyl, phenyl, naphthyl, heteroaryl or the like; R.sup.1 is hydrogen, C.sub.1-6 alkyl or the like; R.sup.2 is hydrogen, C.sub.1-4 alkyl, C(O)R.sup.5 wherein R.sup.5 is C.sub.1-22 alkyl or C.sub.2-22 alkenyl, halosubstituted C.sub.1-8 alkyl, halosubstituted C.sub.2-8 alkenyl, --Y--C.sub.3-7 cycloalkyl, --Y--C.sub.3-7 cycloalkenyl, phenyl, naphthyl, heteroaryl or the like; X is halo, C.sub.1-4 alkyl, hydroxy, C.sub.1-4 alkoxy or the like; and n is 0, 1, 2 or 3, with the proviso that a group of formula --Y--Q is not methyl or ethyl when X is hydrogen; L is oxygen; R.sup.1 is hydrogen; and R.sup.2 is acetyl.

This invention also provides a pharmaceutical composition useful for the treatment of a medical condition in which prostaglandins are implicated as pathogens.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 15 OF 48 USPATFULL on STN
AN 2001:163224 USPATFULL
TI Sulfonylbenzene compounds as anti-inflammatory/analgesic agents
IN Ando, Kazuo, Chita-gun, Japan
Kato, Tomoki, Chita-gun, Japan
Kawai, Akiyoshi, Chita-gun, Japan
Nonomura, Tomomi, Chita-gun, Japan
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 6294558 B1 20010925
WO 9711704 19970403 <--
AI US 1999-446049 19991215 (9)
WO 1999-IB970 19990531
19991215 PCT 371 date
19991215 PCT 102(e) date
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Patel, Sudhaker B.
LREP Richardson, Peter C., Ginsburg, Paul H., Looney, Adrian G.
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 8683
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a compound of the formula: ##STR1##

or its pharmaceutically acceptable salt thereof, wherein A is partially unsaturated or unsaturated five membered heterocyclic, or partially unsaturated or unsaturated five membered carbocyclic, wherein the 4-(sulfonyl)phenyl and the 4-substituted phenyl in the formula (I) are attached to ring atoms of Ring A, which are adjacent to each other; R.sup.1 is optionally substituted aryl or heteroaryl, with the proviso that when A is pyrazole, R.sup.1 is heteroaryl; R.sup.2 is C.sub.1-4 alkyl, halo-substituted C.sub.1-4 alkyl, C.sub.1-4 alkylamino, C.sub.1-4 dialkylamino or amino; R.sup.3, R.sup.4 and R.sup.5 are independently hydrogen, halo, C.sub.1-4 alkyl, halo-substituted C.sub.1-4 alkyl or the like; or two of R.sup.3, R.sup.4 and R.sup.5 are taken together with atoms to which they are attached and form a 4-7 membered ring; R.sup.6

and R.sup.7 are independently hydrogen, halo, C.sub.1-4 alkyl, halo-substituted C.sub.1-4 alkyl, C.sub.1-4 alkoxy, C.sub.1-4 alkylthio, C.sub.1-4 alkylamino or N,N-di C.sub.1-4 alkylamino; and m and n are independently 1, 2, 3 or 4. This invention also provides a pharmaceutical composition useful for the treatment of a medical condition in which prostaglandins are implicated as pathogens.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 16 OF 48 USPATFULL on STN
AN 2001:97936 USPATFULL
TI Cycloalkyl substituted imidazoles
IN Adams, Jerry Leroy, Wayne, PA, United States
Boehm, Jeffrey Charles, King of Prussia, PA, United States
Garigipati, Ravi Shanker, West Warwick, RI, United States
Sorenson, Margaret, Meriden, CT, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6251914 B1 20010626
WO 9901452 19990114 <--
AI US 1999-445857 19991215 (9)
WO 1998-US13800 19980701
19991215 PCT 371 date
19991215 PCT 102(e) date
PRAI US 1997-51510P 19970702 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Dinner, Dara L., Venetianer, Stephen, Kinzig, Charles M.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3108
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel 1,4,5-substituted imidazole compounds and compositions for use in therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 17 OF 48 USPATFULL on STN
AN 2001:60066 USPATFULL
TI Diaryl-2-(5H)-furanones as **Cox-2 inhibitors**
IN Black, Cameron, Kirkland, Canada
Grimm, Erich, Kirkland, Canada
Leger, Serge, Kirkland, Canada
Prasit, Petpiboon, Kirkland, Canada
Wang, Zhaoyin, Kirkland, Canada
PA Merck Frosst Canada & Co., Kirkland, Canada (non-U.S. corporation)
PI US 6222048 B1 20010424
WO 9619469 19960627
AI US 1997-11674 19970612 (9)
WO 1995-CA715 19951218
19970612 PCT 371 date
19970612 PCT 102(e) date
DT Utility
FS Granted
EXNAM Primary Examiner: Higel, Floyd D.
LREP Yuro, Raynard, Rose, David L.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2485
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula (I) as well as a

method of treating cyclooxygenase-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula (I). The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula (I). ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 18 OF 48 USPATFULL on STN
AN 2000:113991 USPATFULL
TI Bicyclic hydroxamic acid derivatives
IN Robinson, Ralph Pelton, Gales Ferry, CT, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 6110964 20000829
WO 9952910 19991021 <--
AI US 1999-402259 19990930 (9)
WO 1999-IB503 19990324
19990930 PCT 371 date
19990930 PCT 102(e) date
PRAI US 1998-81309P 19980410 (60)
US 1997-55208P 19970808 (60)
US 1997-55207P 19970808 (60)
US 1997-62766P 19971024 (60)
US 1997-68261P 19971219 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Richardson, Peter C., Ginsburg, Paul H., Appleman, Polene W.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1851
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the formula ##STR1## wherein Z and Q are as defined in the specification, to pharmaceutical compositions containing them and to their medicinal use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 19 OF 48 USPATFULL on STN
AN 2000:88221 USPATFULL
TI (4-arylsulfonylamino)-tetrahydropyran-4-carboxylic acid hydroxamides
IN Reiter, Lawrence Alan, Mystic, CT, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 6087392 20000711
WO 9952889 19991021 <--
AI US 1999-380436 19990901 (9)
WO 1999-IB505 19990324
19990901 PCT 371 date
19990901 PCT 102(e) date
PRAI US 1998-81364P 19980410 (60)
US 1997-55208P 19970808 (60)
US 1997-55207P 19970808 (60)
US 1997-62766P 19971024 (60)
US 1997-68261P 19971219 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Dentz, Bernard
LREP Richardson, Peter C., Ginsburg, Paul H., Butterfield, Garth
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1377

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of the formula ##STR1## wherein Q is as defined above, are useful in the treatment of a condition selected from the group consisting of arthritis (including osteoarthritis and rheumatoid arthritis), inflammatory bowel disease, Crohn's disease, emphysema, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, **cancer**, tissue ulceration, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joint implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic aneurysm and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neuro-degenerative disorders (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular **angiogenesis**, corneal injury, macular degeneration, abnormal wound healing, burns, diabetes, tumor invasion, tumor growth, tumor metastasis, corneal scarring, scleritis, AIDS, sepsis and septic shock. In addition, the compounds of the present invention may be used in combination therapy with standard non-steroidal anti-inflammatory drugs (NSAID'S) and analgesics, and in combination with cytotoxic drugs such as adriamycin, daunomycin, cis-platinum, etoposide, taxol, taxotere and other alkaloids, such as vincristine, in the treatment of **cancer**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 20 OF 48 USPATFULL on STN

AN 2000:54102 USPATFULL

TI 3,4-Diaryl-2-hydroxy-2,5-dihydrofurans as prodrugs to **cox-2 inhibitors**

IN Black, Cameron, Pointe Claire, Canada
Leger, Serge, Dollard Des Ormeaux, Canada
Prasit, Petpiboon, Kirkland, Canada
Wang, Zhaoyin, Pierrefonds, Canada
Hamel, Pierre, Laval, Canada
Han, Yongxin, Kirkland, Canada
Hughes, Gregory, Bridgewater, Canada

PA Merck Frosst Canada & Co., Kirkland, Canada (non-U.S. corporation)

PI US 6057319 20000502
WO 9716435 19970509

AI US 1998-68139 19981002 (9)
WO 1996-CA717 19961029
19981002 PCT 371 date
19981002 PCT 102(e) date

PRAI US 1995-8074P 19951030 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Sackey, Ebenezer

LREP Billups, Richard C., Rose, David L.

CLMN Number of Claims: 20

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5440

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention encompasses the novel compound of formula (I) useful in the treatment of cyclooxygenase-2 mediated diseases. The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of formula (I). ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 21 OF 48 USPATFULL on STN
AN 1999:167000 USPATFULL
TI Pyridazinones as inhibitors of cyclooxygenase-2
IN Li, Chun Sing, Pointe Claire, Canada
Gauthier, Jacques Y., Laval, Canada
Lau, Cheuk K., Ile Bizard, Canada
Therien, Michel, Laval, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 6004960 19991221 <--
AI US 1998-42174 19980313 (9)
PRAI US 1997-40791P 19970314 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Bernhardt, Emily
LREP Billups, Richard C., Rose, David L.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1907
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating cyclooxygenase-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 22 OF 48 USPATFULL on STN
AN 1999:166990 USPATFULL
TI 2-aminopyridines as inhibitors of cyclooxygenase-2
IN Friesen, Richard, Quebec, Canada
Dube, Daniel, Quebec, Canada
Deschenes, Denis, Quebec, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 6004950 19991221 <--
AI US 1998-151633 19980911 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak
LREP Billups, Richard C., Rose, David L.
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1785
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating cyclooxygenase-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 23 OF 48 USPATFULL on STN
AN 1999:163698 USPATFULL
TI Substituted pyridines as selective cyclooxygenase-2 inhibitors
IN Dube, Daniel, St. Lazare, Canada
Fortin, Rejean, Montreal-Nord, Canada

Friesen, Richard, Dollard des Ormeaux, Canada
Wang, Zhaoyin, Pierrefonds, Canada
Gauthier, Jacques Yves, Laval, Canada
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6001843 19991214 <--
AI US 1998-181887 19981029 (9)
RLI Division of Ser. No. US 1997-893395, filed on 11 Jul 1997, now patented, Pat. No. US 5861419
PRAI US 1996-22128P 19960718 (60)
US 1996-27139P 19961001 (60)
US 1997-41814P 19970408 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Mach, D. Margaret M.
LREP Billups, Richard C., Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2408
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating COX-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. The invention also encompasses certain pharmaceutical compositions for treatment of COX-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 24 OF 48 USPATFULL on STN
AN 1999:151212 USPATFULL
TI Heterocyclo-substituted imidazopyrazine protein tyrosine kinase inhibitors
IN Chen, Ping, Lawrenceville, NJ, United States
Norris, Derek J., Trenton, NJ, United States
Barrish, Joel C., Holland, PA, United States
Iwanowicz, Edwin J., Cranbury, NJ, United States
PA Bristol-Myers Squibb Co., New York, NY, United States (U.S. corporation)
PI US 5990109 19991123 <--
AI US 1999-262525 19990304 (9)
PRAI US 1998-76789P 19980304 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Gerstl, Robert
LREP Sher, Audrey F.
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2747
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel heterocyclo-substituted imidazopyrazines and salts thereof, pharmaceutical compositions containing such compounds, and methods of using such compounds in the treatment of protein tyrosine kinase-associated disorders such as immunologic disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 25 OF 48 USPATFULL on STN
AN 1999:141983 USPATFULL
TI (Methylsulfonyl)phenyl-2-(5H)-furanones as **COX-2 inhibitors**
IN Belley, Michel, Pierrefonds, Canada
Gauthier, Jacques Yves, Laval, Canada
Grimm, Erich, Baie D'Urfe, Canada

LeBlanc, Yves, Kirkland, Canada
Li, Chun-Sing, Dollard Des Ormeaux, Canada
Therien, Michel, Laval, Canada
Black, Cameron, Pointe Claire, Canada
Prasit, Petpiboon, Kirkland, Canada
Lau, Cheuk-Kun, Ile Bizard, Canada
Roy, Patrick, Dollard Des Ormeaux, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5981576 19991109 <--
AI US 1998-97537 19980615 (9)
RLI Continuation-in-part of Ser. No. US 1996-728512, filed on 9 Oct 1996, now abandoned
PRAI US 1995-5371P 19951013 (60)
US 1996-11637P 19960214 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Billups, Richard C., Rose, David L.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4819
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula A that is useful in the treatment of cyclooxygenase-2 mediated diseases. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula A.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 26 OF 48 USPATFULL on STN
AN 1999:81823 USPATFULL
TI Alkylated styrenes as prodrugs to **COX-2 inhibitors**
IN Black, Cameron, Pointe Claire, Canada
Hughes, Greg, Bridgewater, Canada
Grimm, Erich, Baie d'Urfe, Canada
Leger, Serge, Dollard des Ormeaux, Canada
Prasit, Petpiboon, Kirkland, Canada
Wang, Zhaoyin, Pierrefonds, Canada
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5925631 19990720 <--
AI US 1998-128140 19980803 (9)
RLI Division of Ser. No. US 1997-786517, filed on 21 Jan 1997, now patented, Pat. No. US 5789413
PRAI US 1996-10432P 19960201 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
LREP Billups, Richard C., Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2774
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of cyclooxygenase-2 mediated diseases. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 27 OF 48 USPATFULL on STN

AN 1999:78747 USPATFULL
TI Pyridinyl-2-cyclopenten-1-ones as selective cyclooxygenase-2 inhibitors
IN Black, Cameron, Pointe Claire, Canada
Wang, Zhaoyin, Pierrefonds, Canada
Hughes, Greg, Bridgewater, Canada
PA Merck Frosst Canada, Kirkland, Canada (non-U.S. corporation)
PI US 5922742 19990713 <--
AI US 1997-832407 19970402 (8)
PRAI US 1996-16076P 19960423 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Billups, Richard C., Rose, David L.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1406
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating COX-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of COX-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 28 OF 48 USPATFULL on STN
AN 1999:72602 USPATFULL
TI Conjugates of dithiocarbamates with pharmacologically active agents and uses therefore
IN Lai, Ching-San, Encinitas, CA, United States
PA Medinox, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5916910 19990629 <--
AI US 1997-869158 19970604 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Reiter, Esq., Stephen E.Gray, Cary, Ware & Freidenrich
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1842
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In accordance with the present invention, there are provided conjugates of nitric oxide scavengers (e.g., dithiocarbamates, or "DC") and pharmacologically active agents (e.g., NSAIDs). Invention conjugates provide a new class of pharmacologically active agents (e.g., anti-inflammatory agents) which cause a much lower incidence of side-effects due to the protective effects imparted by modifying the pharmacologically active agents as described herein. In addition, invention conjugates are more effective than unmodified pharmacologically active agents because cells and tissues contacted by the pharmacologically active agent(s) are protected from the potentially damaging effects of nitric oxide overproduction induced thereby as a result of the co-production of nitric oxide scavenger (e.g., dithiocarbamate), in addition to free pharmacologically active agent, when invention conjugate is cleaved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 29 OF 48 USPATFULL on STN
AN 1999:19188 USPATFULL
TI Indene inhibitors of COX-2

IN Failli, Amedeo A., Princeton Junction, NJ, United States
PA American Home Products Corporation, Madison, NJ, United States (U.S. corporation)
PI US 5869524 19990209 <--
AI US 1997-959743 19971028 (8)
PRAI US 1996-30863P 19961112 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Morris, Patricia L.
LREP Milowsky, Arnold S.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides compounds of formula 1 having the structure ##STR1## wherein: R.sup.1 is hydrogen, halogen, alkyl, alkoxy, fluoroalkoxy, trifluoromethyl, alkylthio, or SCF.sub.3

R.sup.2 and R.sup.3 are each independently, hydrogen or alkyl, or R.sup.2 and R.sup.3 may be taken together to form a saturated cycloalkyl ring; and

R.sup.4, R.sup.5, R.sup.6, R.sup.7 and R.sup.8 are each independently, hydrogen, alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, halogen, fluoroalkoxy, CF.sub.3, or SCF.sub.3 which are useful in the treatment of arthritic disorders, colorectal **cancer**, and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 30 OF 48 USPATFULL on STN
AN 1999:7406 USPATFULL
TI Substituted pyridines as selective cyclooxygenase-2 inhibitors
IN Dube, Daniel, St. Lazare, Canada
Friesen, Richard, Dollard des Ormeaux, Canada
Fortin, Rejean, Montreal-Nord, Canada
Wang, Zhaoyin, Pierrefonds, Canada
Gauthier, Jacques Yves, Laval, Canada
PA Merck Frosst Canad, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5861419 19990119 <--
AI US 1997-893395 19970711 (8)
PRAI US 1996-22128P 19960718 (60)
US 1996-27139P 19961001 (60)
US 1997-41814P 19970408 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Mach, D. Margaret M.
LREP Billups, Richard C., Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2464
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating COX-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of COX-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 31 OF 48 USPATFULL on STN
AN 1998:135056 USPATFULL
TI Pyranoindole and tetrahydrocarbazole inhibitors of COX-2
IN Failli, Amedeo A., Princeton Junction, NJ, United States
Steffan, Robert J., Langhorne, PA, United States
Kreft, Anthony F., Langhorne, PA, United States
Caggiano, Thomas J., Morrisville, PA, United States
Caufield, Craig E., Princeton Junction, NJ, United States
PA American Home Products Corporation, Madison, NJ, United States (U.S. corporation)
PI US 5830911 19981103 <--
AI US 1997-906361 19970805 (8)
PRAI US 1996-23938P 19960814 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Morris, Patricia L.
LREP Milowsky, Arnold S.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1511
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides compounds of formula I having the structure ##STR1## wherein R is (CH.sub.2).sub.n COOR.sup.4 ;

R.sup.1 is hydrogen, alkyl, alkenyl, alkynyl, alkylcycloalkyl, and alkoxyalkyl;

R.sup.4 is hydrogen or alkyl;

R.sup.5, R.sup.6, R.sup.7, and R.sup.8 are each, independently, hydrogen, halogen, alkyl, alkenyl, alkynyl, alkoxy, arylalkoxy, fluoroalkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, nitro, --SCF.sub.3, --COR.sup.3, alkanoyloxy, hydroxy, trifluoromethyl, amino, alkylamino, dialkylamino, alkylamido, or alkylsulfonamido; wherein at least one of R.sup.5, R.sup.6, R.sup.7, or R.sup.8 is cyano;

R.sup.3 is alkyl, hydroxy, alkoxy, amino, alkylamino;

X is --O-- or --C--; and

n=1-4

or a pharmaceutically acceptable salt thereof, which are useful in the treatment of arthritic disorders, colorectal **cancer**, and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 32 OF 48 USPATFULL on STN
AN 1998:122449 USPATFULL
TI Bisaryl cyclobutenes derivatives as cyclooxygenase inhibitors
IN Dube, Daniel, St. Lazare, Canada
Fortin, Rejean, Montreal-Nord, Canada
Frenette, Richard, Vimont, Canada
Friesen, Richard, Dollard Des Ormeaux, Canada
Guay, Daniel, Ile Perrot, Canada
Prescott, Sylvie, Chomedey, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5817700 19981006 <--
AI US 1997-814388 19970311 (8)
PRAI US 1996-14287P 19960329 (60)
DT Utility
FS Granted

EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Awlakh, Charanjit S.
LREP Billups, Richard C., Rose, David L.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2529
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of cyclooxygenase-2 mediated diseases. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 33 OF 48 USPATFULL on STN
AN 1998:92035 USPATFULL
TI Alkylated styrenes as prodrugs to **COX-2 inhibitors**
IN Black, Cameron, Pointe Claire, Canada
Grimm, Erich, Baie D'Urfe, Canada
Leger, Serge, Dollard Des Ormeaux, Canada
Hughes, Greg, Bridgewater, Canada
Prasit, Petpiboon, Kirkland, Canada
Wang, Zhaoyin, Pierrefonds, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5789413 19980804 <--
AI US 1997-786517 19970121 (8)
PRAI US 1996-10432P 19960201 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak
LREP Billups, Richard C., Rose, David L., Panzer, Curtis C.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2711
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of cyclooxygenase-2 mediated diseases. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 34 OF 48 USPATFULL on STN
AN 1998:33931 USPATFULL
TI Diphenyl stilbenes as prodrugs to **COX-2 inhibitors**
IN Black, Cameron, Pointe Claire, Canada
Girard, Mario, Montreal, Canada
Guay, Daniel, Ile Perrot, Canada
Wang, Zhaoyin, Pierrefonds, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5733909 19980331 <--
AI US 1997-784663 19970121 (8)
PRAI US 1996-10950P 19960201 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.; Assistant Examiner: Oswecki, Jane C.
LREP Billups, Richard C., Rose, David L.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 1279
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of cyclooxygenase-2 mediated diseases. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 35 OF 48 USPATFULL on STN
AN 97:118075 USPATFULL
TI 3,4-diaryl-2-hydroxy-2,5-dihydrofurans as prodrugs to **COX-2 inhibitors**
IN Black, Cameron, Pointe Claire, Canada
Leger, Serge, Dollard des Ormeaux, Canada
Prasit, Petpiboon, Kirkland, Canada
Wang, Zhaoyin, Pierrefonds, Canada
Hamel, Pierre, Laval, Canada
Han, Yongxin, Kirkland, Canada
Hughes, Gregory, Bridgewater, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5698584 19971216 <--
AI US 1996-738143 19961025 (8)
PRAI GB 1996-2877 19960213
DT Utility
FS Granted
EXNAM Primary Examiner: Dentz, Bernard
LREP Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5268
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of cyclooxygenase-2 mediated diseases. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 36 OF 48 USPATFULL on STN
AN 97:109930 USPATFULL
TI Diaryl-5-oxygenated-2-(5H) -furanones as **COX-2 inhibitors**
IN Black, Cameron, Point Claire, Canada
Grimm, Erich, Baie D'Urfe, Canada
Wang, Zhaoyin, Pierrefonds, Canada
Leger, Serge, Dollard des Ormeaux, Canada
PA Merck Frosst Canada Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5691374 19971125 <--
AI US 1995-443620 19950518 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Dentz, Bernard
LREP Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1667
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating cyclooxygenase-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic

therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 37 OF 48 USPATFULL on STN
AN 97:94250 USPATFULL
TI Diphenyl-1,2-3-thiadiazoles as anti-inflammatory agents
IN Lau, Cheuk Kun, Ile Bizard, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5677318 19971014 <--
AI US 1996-678274 19960711 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: McKane, Joseph
LREP Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1050
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating COX-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of COX-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 38 OF 48 USPATFULL on STN
AN 96:80289 USPATFULL
TI Aryl substituted 5,5 fused aromatic nitrogen compounds as anti-inflammatory agents
IN Gauthier, Jacques Y., Laval, Canada
Lau, Cheuk K., Ile Bizard, Canada
LeBlanc, Yves, Kirkland, Canada
Li, Chun-Sing, Dollard des Ormeaux, Canada
Roy, Patrick, Dollard des Ormeaux, Canada
Therien, Michel, Laval, Canada
Wang, Zhaoyin, Pierrefonds, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5552422 19960903 <--
AI US 1995-371179 19950111 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Gerstl, Robert
LREP Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1598
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I as well as a method of treating cyclooxygenase-2 mediated diseases comprising administration to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound of Formula I. ##STR1## The invention also encompasses certain pharmaceutical compositions for treatment of cyclooxygenase-2 mediated diseases comprising compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 39 OF 48 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-620295 [53] WPIDS
DNC C1999-181056
TI Novel method of inducing a cytocidal immune response against preselected cell types such as **cancer** cells or virally infected cells.
DC B04 D16
IN GILLIES, S D
PA (LEXI-N) LEXIGEN PHARM CORP
CYC 86
PI WO 9952562 A2 19991021 (199953)* EN 46<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9935650 A 19991101 (200013) <--
NO 2000005155 A 20001213 (200106)
EP 1071468 A2 20010131 (200108) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE SI
HU 2001001352 A2 20010828 (200157)
CN 1305386 A 20010725 (200164)
BR 9909583 A 20020115 (200214)
CZ 2000003767 A3 20020116 (200215)
ZA 2000005475 A 20020130 (200217) 70
JP 2002511432 W 20020416 (200242) 59
AU 758860 B 20030403 (200335)
ADT WO 9952562 A2 WO 1999-US8335 19990415; AU 9935650 A AU 1999-35650 19990415; NO 2000005155 A WO 1999-US8335 19990415, NO 2000-5155 20001013; EP 1071468 A2 EP 1999-917558 19990415, WO 1999-US8335 19990415; HU 2001001352 A2 WO 1999-US8335 19990415, HU 2001-1352 19990415; CN 1305386 A CN 1999-807249 19990415; BR 9909583 A BR 1999-9583 19990415, WO 1999-US8335 19990415; CZ 2000003767 A3 WO 1999-US8335 19990415, CZ 2000-3767 19990415; ZA 2000005475 A ZA 2000-5475 20001006; JP 2002511432 W WO 1999-US8335 19990415, JP 2000-543172 19990415; AU 758860 B AU 1999-35650 19990415
FDT AU 9935650 A Based on WO 9952562; EP 1071468 A2 Based on WO 9952562; HU 2001001352 A2 Based on WO 9952562; BR 9909583 A Based on WO 9952562; CZ 2000003767 A3 Based on WO 9952562; JP 2002511432 W Based on WO 9952562; AU 758860 B Previous Publ. AU 9935650, Based on WO 9952562
PRAI US 1998-81863P 19980415
AN 1999-620295 [53] WPIDS
AB WO 9952562 A UPAB: 19991215
NOVELTY - A method of inducing a cytocidal immune response against a preselected cell-type in a mammal comprising administering, an immunoconjugate comprising an antibody binding site capable of binding the preselected cell-type and a cytokine capable of inducing the immune response against the preselected cell type, and an **angiogenesis** inhibitor sufficient to enhance the immune response, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of inducing a cytocidal immune response against a **cancer** cell in a mammal comprising administering to the mammal:

(a) an immunoconjugate comprising an antibody binding site capable of binding the **cancer** cell and a cytokine capable of inducing the immune response against the tumor cell; and

(b) an **angiogenesis** inhibitor selected from endostatin and angiostatin to enhance the immune response relative to immunoconjugate alone; and

(2) a composition for inducing an immune response against a preselected cell-type in a mammal comprising in combination:

(a) an immunoconjugate comprising an antibody binding site capable of binding the preselected cell-type and a cytokine capable of inducing an

immune response against the preselected cell-type in the mammal; and
(b) an **angiogenesis** inhibitor to enhance the immune response induced by the immunoconjugate of the combination relative to immunoconjugate alone.
ACTIVITY - Cytostatic; antiviral.
MECHANISM OF ACTION - Immunoconjugate.
USE - The method can be used for inducing a cytocidal immune response against a preselected cell-type such as a **cancer** cell or a virus-infected cell (claimed).
Dwg.0/5

L11 ANSWER 40 OF 48 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1998-609965 [51] WPIDS
CR 2000-339626 [29]; 2000-452130 [39]; 2000-452291 [39]; 2000-452303 [39]; 2000-452304 [39]; 2000-452305 [39]; 2000-452306 [39]; 2000-452307 [39]; 2000-452313 [39]; 2000-475624 [41]
DNC C1998-182797
TI New substituted benzopyran derivatives and analogues - are useful for treating cyclooxygenase-2-mediated disorders, e.g. inflammation, arthritis, pain and fever.
DC B05
IN BERTENSHAW, S R; BROWN, D L; CARTER, J S; DEVADAS, B; GRANETO, M J; HANAU, C E; HARTMANN, S J; LUDWIG, C L; METZ, S; NAGARAJAN, S R; OBUKOWICZ, M G; ROGIER, D J; TALLEY, J J; KORTE, D E; MASFERRER, J L
PA (SEAR) SEARLE & CO G D; (PHAA) PHARMACIA CORP
CYC 84
PI WO 9847890 A1 19981029 (199851)* EN 294<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9871256 A 19981113 (199913) <--
ZA 9803287 A 19990630 (199931) 290<--
EP 977748 A1 20000209 (200012) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 9905113 A 19991221 (200012) <--
US 6034256 A 20000307 (200019)
US 6077850 A 20000620 (200035)
BR 9808953 A 20000801 (200043)
CN 1257489 A 20000621 (200049)
CZ 9903673 A3 20000913 (200054)
SK 9901386 A3 20001009 (200056)
NZ 500387 A 20010223 (200115)
US 6271253 B1 20010807 (200147)
KR 2001020152 A 20010315 (200157)
AU 742033 B 20011213 (200210)
US 2002010206 A1 20020124 (200210)
HU 2000001352 A2 20020128 (200222)
JP 2002511062 W 20020409 (200227) 396
MX 9909690 A1 20010501 (200227)
US 6492390 B2 20021210 (200301)
EP 977748 B1 20030326 (200323) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 69812603 E 20030430 (200336)
ES 2194314 T3 20031116 (200381)
US 2004038977 A1 20040226 (200416)
US 2004072889 A1 20040415 (200426)
ADT WO 9847890 A1 WO 1998-US7677 19980418; AU 9871256 A AU 1998-71256 19980418; ZA 9803287 A ZA 1998-3287 19980420; EP 977748 A1 EP 1998-918305 19980418, WO 1998-US7677 19980418; NO 9905113 A WO 1998-US7677 19980418,

NO 1999-5113 19991020; US 6034256 A Provisional US 1997-44485P 19970421, US 1998-62537 19980417; US 6077850 A Provisional US 1997-44485P 19970421, CIP of US 1998-62537 19980417, US 1998-175584 19981020; BR 9808953 A BR 1998-8953 19980418, WO 1998-US7677 19980418; CN 1257489 A CN 1998-805255 19980418; CZ 9903673 A3 WO 1998-US7677 19980418, CZ 1999-3673 19980418; SK 9901386 A3 WO 1998-US7677 19980418, SK 1999-1386 19980418; NZ 500387 A NZ 1998-500387 19980418, WO 1998-US7677 19980418; US 6271253 B1 Provisional US 1997-44485P 19970421, CIP of US 1998-62537 19980417, Cont of US 1998-175584 19981020, US 2000-569383 20000511; KR 2001020152 A KR 1999-709710 19991021; AU 742033 B AU 1998-71256 19980418; US 2002010206 A1 Provisional US 1997-44485P 19970421, CIP of US 1998-62537 19980417, Cont of US 1998-175584 19981020, Cont of US 2000-569383 20000511, US 2001-865177 20010524; HU 2000001352 A2 WO 1998-US7677 19980418, HU 2000-1352 19980418; JP 2002511062 W JP 1998-546167 19980418, WO 1998-US7677 19980418; MX 9909690 A1 MX 1999-9690 19991021; US 6492390 B2 Provisional US 1997-44485P 19970421, CIP of US 1998-62537 19980417, Cont of US 1998-175584 19981020, Cont of US 2000-569383 20000511, US 2001-865177 20010524; EP 977748 B1 EP 1998-918305 19980418, WO 1998-US7677 19980418; DE 69812603 E DE 1998-612603 19980418, EP 1998-918305 19980418, WO 1998-US7677 19980418; ES 2194314 T3 EP 1998-918305 19980418; US 2004038977 A1 Provisional US 1997-44485P 19970421, CIP of US 1998-62537 19980417, Cont of US 1998-175584 19981020, Cont of US 2000-569383 20000511, Cont of US 2001-865177 20010524, US 2002-303150 20021122; US 2004072889 A1 Provisional US 1997-44485P 19970421, CIP of US 1998-62537 19980417, Cont of US 1998-175584 19981020, Provisional US 1998-113786P 19981223, CIP of US 1999-470951 19991222, Cont of US 2000-569383 20000511, CIP of US 2001-865177 20010524, US 2003-414867 20030416

FDT AU 9871256 A Based on WO 9847890; EP 977748 A1 Based on WO 9847890; BR 9808953 A Based on WO 9847890; CZ 9903673 A3 Based on WO 9847890; NZ 500387 A Based on WO 9847890; US 6271253 B1 CIP of US 6034256, Cont of US 6077850; AU 742033 B Previous Publ. AU 9871256, Based on WO 9847890; US 2002010206 A1 CIP of US 6034256, Cont of US 6077850, Cont of US 6271253; HU 2000001352 A2 Based on WO 9847890; JP 2002511062 W Based on WO 9847890; US 6492390 B2 CIP of US 6034256, Cont of US 6077850, Cont of US 6271253; EP 977748 B1 Based on WO 9847890; DE 69812603 E Based on EP 977748, Based on WO 9847890; ES 2194314 T3 Based on EP 977748; US 2004038977 A1 CIP of US 6034256, Cont of US 6077850, Cont of US 6271253, Cont of US 6492390; US 2004072889 A1 CIP of US 6034256, Cont of US 6077850, Cont of US 6271253, CIP of US 6492390

PRAI US 1997-44485P 19970421; US 1998-62537 19980417;
US 1998-175584 19981020; US 2000-569383 20000511;
US 2001-865177 20010524; US 2002-303150 20021122;
US 1998-113786P 19981223; US 1999-470951 19991222;
US 2003-414867 20030416

AN 1998-609965 [51] WPIDS

CR 2000-339626 [29]; 2000-452130 [39]; 2000-452291 [39]; 2000-452303 [39]; 2000-452304 [39]; 2000-452305 [39]; 2000-452306 [39]; 2000-452307 [39]; 2000-452313 [39]; 2000-475624 [41]

AB WO 9847890 A UPAB: 20040421

Substituted benzopyran derivatives (including aza, benzothiopyran, naphthalene and quinoline analogues) of formula (I) and their salts are new. X = O, S, CRcRd or NRa; Ra = H, 1-3C alkyl, optionally substituted phenyl-(1-3C) alkyl, acyl or carboxy-(1-6C) alkyl; Rb,Rc = H, 1-3C alkyl, phenyl-(1-3C) alkyl, 1-3C perfluoroalkyl, Cl, 1-6C alkylthio, 1-6C alkoxy, NO2, CN or cyano-(1-3C) alkyl; R = COOH, NH2CO, (1-6C) alkylsulphonylaminocarbonyl or (1-6C) alkoxycarbonyl; R'' = H, phenyl, thienyl or 2-6C alkenyl; R1 = 1-3C perfluoroalkyl, Cl, 1-6C alkylthio, 1-6C alkoxy, NO2, CN or 1-3C cyanoalkyl; R2 = H, halo, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 2-6C haloalkynyl, aryl-(1-3C) alkyl, aryl-(2-6C) alkynyl, aryl-(2-6C) alkenyl, 1-6C alkoxy, methylenedioxy, 1-6C alkylthio, 1-6C alkylsulphinyl, aryloxy, arylthio, arylsulphinyl, heteroaryloxy, 1-6C alkoxy-(1-6C) alkyl, aryl-(1-6C) alkoxy, heteroaryl-(1-6C) alkoxy, aryl-(1-6C) alkoxy-(1-6C) alkyl, 1-6C haloalkyl, 1-6C haloalkoxy, 1-6C haloalkylthio, 1-6C haloalkylsulphinyl, 1-6C haloalkylsulphonyl, 1-3C

haloalkyl-(1-3C) hydroxyalkyl, 1-6C hydroxyalkyl, hydroxyimino-(1-6C) alkyl, 1-6C alkylamino, arylamino, aryl-(1-6C) alkylamino, heteroarylamino, heteroaryl-(1-6C) alkylamino, NO2, CN, NH2, NH2SO2, 1-6C alkylaminosulphonyl, arylaminosulphonyl, heteroarylaminosulphonyl, aryl-(1-6C) alkylaminosulphonyl, heteroaryl-(1-6C) alkylaminosulphonyl, heterocyclylsulphonyl, 1-6C alkylsulphonyl, aryl-(1-6C) alkylsulphonyl, optionally substituted aryl, optionally substituted heteroaryl, aryl-(1-6C) alkylcarbonyl, heteroaryl-(1-6C) alkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, NH2CO, 1-6C alkoxycarbonyl, CHO, 1-6C haloalkylcarbonyl or 1-6C alkylcarbonyl; or R2 together with the ring to which it is attached forms naphthyl, quinolyl, isoquinolyl, quinolizinyl, quinoxalinyl or dibenzofuryl; A1-A4 = C or N, provided that at least two are C-atoms. Alternatively in (I): A1-A4 = C; X = O, S or NRa; Ra = alkyl; R = COOH, NH2CO, alkylsulphonylaminocarbonyl or alkoxycarbonyl; R1 = haloalkyl, alkyl, aralkyl, cycloalkyl or aryl optionally substituted by alkylthio, NO2 or alkylsulphonyl; R2 = H, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, NO2, NH2, aminosulphonyl, alkylaminosulphonyl, arylaminosulphonyl, heteroarylaminosulphonyl, aralkylaminosulphonyl, heteroaralkylaminosulphonyl, heterocyclosulphonyl, alkylsulphonyl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl or alkylcarbonyl; or R2 together with the ring to which it is attached forms naphthyl.

USE - (I) are cyclooxygenase-2 (**COX-2**) **inhibitors**. They are useful for treating COX-2 mediated disorders, specifically inflammation, arthritis, pain and fever (all claimed). Numerous COX-mediated disorders which may be treated are given in the disclosure, including e.g. rheumatoid arthritis, systemic lupus erythematosus, asthma, bronchitis, menstrual cramps, hepatitis, psoriasis, eczema, post-operative inflammation, Crohn's disease, gastritis, irritable bowel syndrome, migraine, aplastic anaemia, Hodgkin's disease, myasthenia gravis, multiple sclerosis, gingivitis, nephritis, retinitis, conjunctivitis, Alzheimer's disease, CNS damage due to stroke or ischaemia, allergic rhinitis, pain of numerous types, dementia, inflammation-related cardiovascular disorders (e.g. vascular disease, coronary artery disease, aneurysm, arteriosclerosis, atherosclerosis, myocardial infarction, embolism, stroke, thrombosis and angina) and **angiogenesis**-related disorders (e.g. neoplasia, **cancer**, metastasis, corneal graft rejection, diabetic retinopathy, glaucoma, gastric ulcers and endometriosis).

ADVANTAGE - (I) selectively inhibit COX-2 over COX-1. They are safer and have less side-effects than conventional NSAID's.

Dwg.0/0

L11 ANSWER 41 OF 48 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1998-531549 [45] WPIDS
DNC C1998-159416
TI New 5-(4-sulphonyl-phenyl)-pyridazinone derivatives - are selective cyclo-oxygenase 2 inhibitors used for treating inflammatory disease, Alzheimer's disease and glaucoma.
DC B03
IN GAUTHIER, J Y; LAU, C K; LI, C S; PRASIT, P; THERIEN, M
PA (MERI) MERCK FROSST CANADA & CO; (MERI) MERCK FROSST CANADA INC
CYC 81
PI WO 9841511 A1 19980924 (199845)* EN 87<--
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GW HU ID IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU
AU 9864913 A 19981012 (199907) <--
US 6004960 A 19991221 (200006) <--

EP 975604 A1 20000202 (200011) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
JP 2001514669 W 20010911 (200167) 94
AU 738727 B 20010927 (200170)

ADT WO 9841511 A1 WO 1998-CA233 19980312; AU 9864913 A AU 1998-64913 19980312; US 6004960 A Provisional US 1997-40791P 19970314, US 1998-42174 19980313; EP 975604 A1 EP 1998-910544 19980312, WO 1998-CA233 19980312; JP 2001514669 W JP 1998-539982 19980312, WO 1998-CA233 19980312; AU 738727 B AU 1998-64913 19980312

FDT AU 9864913 A Based on WO 9841511; EP 975604 A1 Based on WO 9841511; JP 2001514669 W Based on WO 9841511; AU 738727 B Previous Publ. AU 9864913, Based on WO 9841511

PRAI GB 1997-7487 19970414; US 1997-40791P 19970314; US 1998-42174 19980313

AN 1998-531549 [45] WPIDS

AB WO 9841511 A UPAB: 19981111

Pyridazinone derivatives of formula (I) are new: X = a bond, (CH2)m, CO, O, S or NR5; m = 1-2; R1 = Me, NH2 or NHCOCF3; R2 = (CR6R7)nR8; n = 0-2; R6, R7 = H, 1-10C alkyl or 1-10C fluoroalkyl; R3, R8 = 1-10C alkyl, Ph or naphthyl (both optionally substituted by 1-3 of halo 1-10C alkoxy, 1-10C alkylthio, CN, 1-6C fluoroalkyl, 1-10C alkyl or N3) or heteroaryl comprising a monocyclic 5 membered aromatic ring optionally containing one of S, O and N and optionally 1-3 additional N atoms or a 6 membered ring containing 1N and optionally 1-3 additional N atoms (both optionally substituted by halo, 1-10C alkoxy, 1-10C alkylthio, CN, 1-6C fluoroalkyl, 1-10C alkyl or N3); R4 = H, halo or 1-6C alkyl and R5 = H or 1-6C alkyl.

36 Compounds (I) are specifically claimed e.g: 5-(4-methylsulphonyl)-phenyl-2-phenyl-4-phenyl-2H-pyridazin-3-one.

USE - (I) are cyclooxygenase inhibitors which selectively inhibit COX-2 over COX-1 and are useful for treatment of disorders susceptible to treatment with **COX-2 inhibitors** and/or non steroidal antiinflammatory drugs (NSAIDs), particularly pain, fever and inflammation of conditions including rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), gout and ankylosing spondylitis, bursitis, burns, injuries, following surgical and dental procedures. (I) also inhibit cellular neoplastic transformations and metastatic tumour growth and can be used in the treatment of **cancer**. (I) are also used to treat and/or prevent COX-mediated proliferative disorders such as may occur in diabetic retinopathy and tumour **angiogenesis**. (I) also inhibit prostanoid-induced smooth muscle contraction by preventing synthesis of contractile prostanoids and are useful in the treatment of dysmenorrhoea, premature labour, asthma and eosinophil related disorders. (I) are also useful in the treatment of Alzheimer's disease and for prevention of bone loss (treatment of osteoporosis) and treatment of glaucoma. (I) are useful as alternatives to conventional NSAIDs, particularly where NSAIDs are contraindicated e.g. in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of gastrointestinal lesions, gastrointestinal bleeding, coagulation disorders including anaemia such as hypoprothrombinaemia, haemophilia or other bleeding problems, kidney disease and those prior to surgery or taking anticoagulants. (I) can be coadministered with other active agents. The dosage of (I) is 0.01-140 mg/kg/day orally, topically, parenterally, by inhalation spray or rectally. The dosage for treating inflammation is 0.01-50 mg/kg/day.

Dwg.0/0

L11 ANSWER 42 OF 48 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1998-521151 [44] WPIDS

CR 1994-217755 [26]; 1995-051970 [07]; 1995-172512 [23]; 1995-255022 [33]; 1996-221734 [22]; 1997-245037 [22]; 1997-280687 [25]; 1997-435662 [41];

1998-458786 [40]
DNC C1998-156556
TI New (methylsulphonyl)phenyl-2-(5H)-furanone derivatives - are selective cyclooxygenase 2 inhibitors, useful as antiinflammatory, antipyretic and analgesic agents.
DC B03
IN GRIMM, E; LEBLANC, Y; LEGER, S; ROY, P; WANG, Z
PA (MERI) MERCK FROSST CANADA & CO; (MERI) MERCK FROSST CANADA INC
CYC 81
PI WO 9841516 A1 19980924 (199844)* EN 69<--
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GW HU ID IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU
AU 9867142 A 19981012 (199907) <--
EP 970067 A1 20000112 (200008) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
US 6071954 A 20000606 (200033)
JP 2001514668 W 20010911 (200167) 72
AU 741981 B 20011213 (200210)
EP 970067 B1 20030702 (200345) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
DE 69816047 E 20030807 (200359)
ES 2201466 T3 20040316 (200424)
ADT WO 9841516 A1 WO 1998-CA225 19980312; AU 9867142 A AU 1998-67142 19980312; EP 970067 A1 EP 1998-912164 19980312, WO 1998-CA225 19980312; US 6071954 A Provisional US 1997-40794P 19970314, US 1998-42168 19980313; JP 2001514668 W JP 1998-539978 19980312, WO 1998-CA225 19980312; AU 741981 B Div ex AU 1996-71236 19961009, Div ex AU 1996-72736 19961029, AU 1998-67142 19980312; EP 970067 B1 EP 1998-912164 19980312, WO 1998-CA225 19980312; DE 69816047 E DE 1998-616047 19980312, EP 1998-912164 19980312, WO 1998-CA225 19980312; ES 2201466 T3 EP 1998-912164 19980312
FDT AU 9867142 A Based on WO 9841516; EP 970067 A1 Based on WO 9841516; JP 2001514668 W Based on WO 9841516; AU 741981 B Div ex AU 703871, Div ex AU 711902, Previous Publ. AU 9867142, Based on WO 9841516; EP 970067 B1 Based on WO 9841516; DE 69816047 E Based on EP 970067, Based on WO 9841516; ES 2201466 T3 Based on EP 970067
PRAI GB 1997-7488 19970414; US 1997-40794P 19970314; US 1998-42168 19980313
AN 1998-521151 [44] WPIDS
CR 1994-217755 [26]; 1995-051970 [07]; 1995-172512 [23]; 1995-255022 [33]; 1996-221734 [22]; 1997-245037 [22]; 1997-280687 [25]; 1997-435662 [41]; 1998-458786 [40]
AB WO 9841516 A UPAB: 20040408
Methyl sulphonyl)phenyl-2-(5H)-furanone derivatives of formula (I) are new: R = 1-12C alkyl substituted by 1-3 Q, or 2-10C alkenyl 2-10C alkynyl, 3-12C cycloalkenyl or 5-12C cycloalkynyl (all optionally substituted by 1-3 Q); Q = F, Cl, Br, I, OH, CF3, 3-6C cycloalkyl, O, dioxolane or CN; R1 = Me, NH2, NHCOCF3 or NHMe; R2, R3 = H or 1-10C alkyl; or CR2R3 = 3-7C saturated monocyclic ring.

USE - (I) are cyclooxygenase inhibitors which selectively inhibit COX-2 over COX-1 and are useful for treatment of disorders susceptible to treatment with **COX-2 inhibitors** and/or NSAIDs, eg rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), gout and ankylosing spondylitis, bursitis, burns, injuries, following surgical and dental procedures. In addition the compounds inhibit cellular neoplastic transformations and metastatic tumour growth and can be used in the treatment of **cancer**. They may also be used to treat and/or prevent COX-mediated proliferative disorders such as may occur in diabetic retinopathy and tumour

angiogenesis. (I) also inhibit prostanoid-induced smooth muscle contraction by preventing synthesis of contractile prostanoid s and are useful in the treatment of dysmenorrhoea, premature labour, asthma and eosinophil related disorders. (I) are also useful in the treatment of Alzheimer's disease and for prevention of bone loss (treatment of osteoporosis) and treatment of glaucoma. By virtue of their high selectivity for COX-2 over COX-1, (I) are useful as alternatives to conventional NSAIDs, particularly where NSAIDs are contraindicated eg in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of gastrointestinal lesions, GI bleeding, coagulation disorders including anaemia such as hypoprothrombinaemia, haemophilia or other bleeding problems, kidney disease and those prior to surgery or taking anticoagulants. (I) can be coadministered with other active agents.
Dwg.0/0

L11 ANSWER 43 OF 48 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1997-245037 [22] WPIDS
CR 1994-217755 [26]; 1995-051970 [07]; 1995-172512 [23]; 1995-255022 [33]; 1996-221734 [22]; 1997-280687 [25]; 1997-435662 [41]; 1998-458786 [40]; 1998-521151 [44]
DNC C1997-079385
TI 3-phenyl furanone derivatives and their analogues - are specific cyclooxygenase-2 inhibitors, useful for treating pain and inflammatory disorders.
DC B05
IN BELLEY, M; BLACK, C; GAUTHIER, J Y; GRIMM, E; LAU, C; LEBLANC, Y; LI, C; PRASIT, P; ROY, P; THERIEN, M; LAU, C K; THIEREN, M
PA (MERI) MERCK FROSST CANADA INC; (MERI) MERCK FROSST CANADA & CO
CYC 76
PI WO 9714691 A1 19970424 (199722)* EN 264<--
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE HU IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN
ZA 9608609 A 19970625 (199731) 153<--
AU 9671236 A 19970507 (199735) <--
NO 9801628 A 19980527 (199831) <--
EP 863891 A1 19980916 (199841) EN <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT SE SI
CZ 9801101 A3 19980916 (199843) <--
SK 9800450 A3 19981202 (199907) <--
JP 11500146 W 19990106 (199911) 283<--
CN 1200119 A 19981125 (199915) <--
AU 703871 B 19990401 (199925) <--
HU 9802506 A2 19990528 (199930) <--
US 5981576 A 19991109 (199954) <--
BR 9611015 A 19990914 (200004) <--
US 6020343 A 20000201 (200013)
NZ 319090 A 20000128 (200015)
MX 9802836 A1 19980901 (200017) <--
NZ 332820 A 20000526 (200033)
KR 99064265 A 19990726 (200044) <--
US 6169188 B1 20010102 (200103)
JP 2001199954 A 20010724 (200147) 134
TW 426679 A 20010321 (200151)
IL 123699 A 20020310 (200239)
JP 3337476 B2 20021021 (200272) 130
SK 282639 B6 20021008 (200276)
EP 863891 B1 20021211 (200282) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT SE SI
DE 69625374 E 20030123 (200315)
KR 354940 B 20030124 (200339)

ES 2187675 T3 20030616 (200345)
HU 222785 B1 20031028 (200379)
CA 2233178 C 20031223 (200404) EN

ADT WO 9714691 A1 WO 1996-CA682 19961009; ZA 9608609 A ZA 1996-8609 19961011; AU 9671236 A AU 1996-71236 19961009; NO 9801628 A WO 1996-CA682 19961009, NO 1998-1628 19980408; EP 863891 A1 EP 1996-932417 19961009, WO 1996-CA682 19961009; CZ 9801101 A3 WO 1996-CA682 19961009, CZ 1998-1101 19961009; SK 9800450 A3 WO 1996-CA682 19961009, SK 1998-450 19961009; JP 11500146 W WO 1996-CA682 19961009, JP 1997-515371 19961009; CN 1200119 A CN 1996-197609 19961009; AU 703871 B AU 1996-71236 19961009; HU 9802506 A2 WO 1996-CA682 19961009, HU 1998-2506 19961009; US 5981576 A Provisional US 1995-5371P 19951013, Provisional US 1996-11637P 19960214, CIP of US 1996-728512 19961009, US 1998-97537 19980615; BR 9611015 A BR 1996-11015 19961009, WO 1996-CA682 19961009; US 6020343 A Provisional US 1995-5371P 19951013, Provisional US 1996-11637P 19960214, CIP of US 1996-728512 19961009, US 1998-97543 19980615; NZ 319090 A NZ 1996-319090 19961009, WO 1996-CA682 19961009; MX 9802836 A1 MX 1998-2836 19980408; NZ 332820 A Div ex NZ 1996-319090 19961009, NZ 1996-332820 19961009; KR 99064265 A WO 1996-CA682 19961009, KR 1998-702755 19980413; US 6169188 B1 Provisional US 1995-5371P 19951013, Provisional US 1996-11637P 19960214, CIP of US 1996-728512 19961009, Div ex US 1998-97543 19980615, US 1999-422151 19991021; JP 2001199954 A Div ex JP 1997-515371 19961009, JP 2000-366579 19961009; TW 426679 A TW 1996-112463 19961012; IL 123699 A IL 1996-123699 19961009; JP 3337476 B2 WO 1996-CA682 19961009, JP 1997-515371 19961009; SK 282639 B6 WO 1996-CA682 19961009, SK 1998-450 19961009; EP 863891 B1 EP 1996-932417 19961009, WO 1996-CA682 19961009; DE 69625374 E DE 1996-625374 19961009, EP 1996-932417 19961009, WO 1996-CA682 19961009; KR 354940 B WO 1996-CA682 19961009, KR 1998-702755 19980413; ES 2187675 T3 EP 1996-932417 19961009; HU 222785 B1 WO 1996-CA682 19961009, HU 1998-2506 19961009; CA 2233178 C CA 1996-2233178 19961009, WO 1996-CA682 19961009

FDT AU 9671236 A Based on WO 9714691; EP 863891 A1 Based on WO 9714691; CZ 9801101 A3 Based on WO 9714691; JP 11500146 W Based on WO 9714691; AU 703871 B Previous Publ. AU 9671236, Based on WO 9714691; HU 9802506 A2 Based on WO 9714691; BR 9611015 A Based on WO 9714691; NZ 319090 A Based on WO 9714691; NZ 332820 A Div ex NZ 319090; KR 99064265 A Based on WO 9714691; US 6169188 B1 Div ex US 6020343; IL 123699 A Based on WO 9714691; JP 3337476 B2 Previous Publ. JP 11500146, Based on WO 9714691; SK 282639 B6 Previous Publ. SK 9800450, Based on WO 9714691; EP 863891 B1 Based on WO 9714691; DE 69625374 E Based on EP 863891, Based on WO 9714691; KR 354940 B Previous Publ. KR 99064265, Based on WO 9714691; ES 2187675 T3 Based on EP 863891; HU 222785 B1 Based on WO 9714691; CA 2233178 C Based on WO 9714691

PRAI GB 1996-5645 19960318; US 1995-5371P 19951013;
GB 1996-2939 19960213; US 1996-11637P 19960214;
US 1996-728512 19961009; US 1998-97537 19980615;
US 1998-97543 19980615; US 1999-422151 19991021

AN 1997-245037 [22] WPIDS

CR 1994-217755 [26]; 1995-051970 [07]; 1995-172512 [23]; 1995-255022 [33]; 1996-221734 [22]; 1997-280687 [25]; 1997-435662 [41]; 1998-458786 [40]; 1998-521151 [44]

AB WO 9714691 A UPAB: 20040115

3-phenyl-furanone derivatives and their sulphonamide, phosphonamide, phosphinate, or other analogues, of formula (I), and their salts, are new. Y = O, S, CO, or CR11R12; X = CH2, CO, CHOH, O, S, or NR15, provided that, when R3, R4 are other than both H or both alkyl, or CR3R4 together forms a ring, then X = CO, O, S, or NR15; R1 = SO2Me, SO2NR16R17, SO2NHCOCF3, SO(NH)NH2, SO(NH)NHCOCF3, PO(NH2)Me, or POMe2; R2 = 1-10C alkyl, phenyl or naphthyl (both optionally substituted by 1-3 of J, COOH, 2-11C alkoxycarbonyl, (CR5R6)-O-(1-4C alkyl), (1-6C alkyl)COOR5, benzyloxy, O-(1-6C alkyl)COOR5, or O-(1-6C alkyl)NR5R6), or Het1, Het2, Het3, Het4, or Bcb; Het1 = 5- or 6- membered monocyclic heteroaryl containing one O, S, or N atom and optionally 1-3 additional N atoms (optionally substituted by 1-3 of J, CF3, or (CR5R6)-O-(1-10C alkyl)); Het2 = benzoheterocyclyl with a 5-7 membered hetero ring, containing 1 or 2 atoms from O, S, N, and

optionally also a CO or SO2 group (optionally containing 1 or 2 substituents as for Het1); Het3 = 8-10 membered bicyclic heteroaryl, both rings having heteroatom(s), containing 2-5 atoms from N, O, S (optionally substituted by 1 or 2 substituents as for Het1); Het4 = 5-7 membered heterocycloalkyl, optionally containing a CO or SO2 group; Bcb = benzocarbocyclyl with a 5-7 membered carbocyclyl ring containing optionally a CO group (optionally substituted by 1 or 2 substituents as for Het1); R3 = H, 1-10C alkyl, CH2OR7, cyano, cyanomethyl, CON(R7)2, F, 1-6C fluoroalkyl, or phenyl, benzyl, heteroaryl, or heteroarylmethyl (all optionally substituted as for Het1); R4 = H, 1-10C alkyl, alkoxy, or alkylthio, OH, OCOR7, SH, SCOR7, OCOOR8, SCOOR8, OCON(R7)2, SCON(R7)2 or 1-6C fluoroalkyl; or CR3R4= 3-7C cycloalkyl; R5, R6 = H or 1-10C alkyl; or CR5R6 together = 3-7C cycloalkyl; R7 = H, 1-6C alkyl, or phenyl or benzyl (both optionally monosubstituted by halo, cyano, CF3, or 1-6C alkyl, alkoxy, or alkylthio); or N(R7)2 = 5-7 membered saturated azacyclyl; R8 = as for R7, excluding H; R9, R10 = H or 1-7C alkyl; or CR9R10 = CO or CS; R11, R12 = H, 1-7C alkyl, CH2OR7, cyano, cyanomethyl, 1-6C fluoroalkyl, F, OR7, or phenyl, benzyl, heteroaryl, or heteroarylmethyl (all optionally mono- or di- substituted by halo, 1-6C alkyl, alkoxy, or alkylthio, cyano, CF3, azido, (CR13R14)-OH, (CR13R14)-O-(1-4C alkyl), or 1-6C fluoroalkyl; or R13+R14 = 3-7C cycloalkyl; R13, R14 = H or 1-7C alkyl; or CR13R14 = CO, CS, or 3-7C cycloalkyl; R15 = H, or as R2, excluding Bcb, except that the substituent (CR5R6)-O-alkyl in phenyl, naphthyl, and Het3 is limited to 1-4C alkyl; and R16, R17 = H, 1-10C alkyl, alkanoic acid, or alkylamine, or phenyl or benzyl (both optionally monosubstituted by halo, or 1-10C alkyl, alkoxy, alkylthio, alkanoic acid, or alkylamine, or cyano, COOH, or CF3); or NR16R17 = 5-7 membered saturated azacyclyl, optionally containing an additional O, S, or NR5; J = halo, 1-10C alkoxy, 1-10C alkylthio, CN, 1-6C fluoroalkyl, 1-10C alkyl, N3, CO2H or CO2-1-10C alkyl.

USE - (I) are cyclooxygenase (COX) inhibitors, selective for COX-2 in preference to COX-1. They are of use for relief of pain, inflammation, and fever in a variety of conditions, with a profile similar to that of non-steroidal antiinflammatory drugs (NSAIDs). Examples are treatment of rheumatic fever, symptoms associated with influenza, other viral infections, or common cold; ache in back, neck, head, or teeth, sprains, strains, or other injuries, dysmenorrhoea, myositis, neuralgia, synovitis, rheumatoid arthritis, osteoarthritis, gout, ankylosing spondylitis, bursitis, burns, or after surgical or dental procedures. (I) may also inhibit cellular neoplastic change and metastases and be of use in treatment of **cancer**; COX-mediated proliferative disorders, including diabetic retinopathy and tumour **angiogenesis**; of premature labour, asthma, eosinophil mediated disorders, Alzheimer's disease, prevention of bone loss in osteoporosis, particularly in post-menopausal women, and treatment of glaucoma.

ADVANTAGE - As selective **COX-2 inhibitors**, (I) should have less renal or gastrointestinal toxicity, effect on bleeding times than the NSAIDs. (I) should also have less tendency to induce asthma attacks in aspirin sensitive subjects.

Dwg.0/0

L11 ANSWER 44 OF 48 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1997-021121 [02] WPIDS
DNC C1997-006833
TI New N-benzyl-indolyl-propanoic acid derivs. - are selective cyclo-oxygenase-2 inhibitors, especially useful as antiinflammatory agents with reduced side-effects.
DC B02
IN BLACK, C; DUCHARME, Y; GAUTHIER, J; GUAY, D; HAMEL, P; LAU, C K; LEBLANC, Y; ROY, P; GAUTHIER, J Y
PA (MERI) MERCK FROSST CANADA INC
CYC 69
PI WO 9637469 A1 19961128 (199702)* EN 94<--
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG

W: AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IS JP KG KR KZ LK LR LT
LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN
AU 9656832 A 19961211 (199713) <--
US 5604253 A 19970218 (199713) 29<--
ADT WO 9637469 A1 WO 1996-CA326 19960521; AU 9656832 A AU 1996-56832 19960521;
US 5604253 A US 1995-445624 19950522
FDT AU 9656832 A Based on WO 9637469
PRAI US 1995-445624 19950522
AN 1997-021121 [02] WPIDS
AB WO 9637469 A UPAB: 19970108
N-Benzyl-2-methylindol-3-yl propanoic acid derivs. of formula (I) and their salts are new.Q = OR or NR9R10; R = H or 1-4C alkyl; R1 = OMe, OCH2F, OCHF2, F, Cl, Br, I, Me or Et; R2-R5 = H, F, Me, Et, CF3, CHF2, CFH2, OH, OR8, SR8, SOR8, SO2R8, benzyl (opt. mono- or disubstd. by Y') or naphthylmethyl; or R2 + R3 or R4 + R5 = O; or two of R2-R5 together complete a 3-7 membered saturated monocyclic hydrocarbon ring; R6 = H or F ; R7 = Br, Cl, I, SMe, SEt or SCF2H; R8 = Me, Et or benzyl (opt. mono- or disubstd. by Y); R9, R10 = H, 1-3C alkyl, OR, COR11 or SO2R12; 2-4C alkyl monosubstd. (on a C other than that attached to the N) by OH, NH2, NHMe or N(Me)2; or phenyl, benzyl or pyridyl, all opt. mono- or disubstd. by Y; or NR9R10 = 3-7 membered opt. unsatd. monocyclic heterocycle, opt. containing 1 or 2 additional heteroatom(s) selected from N, O and S and opt. containing 1 or 2 CO or SO2 gps.; R11 = H, 1-4C alkyl, CF3 or phenyl or benzyl (both opt. mono- or disubstd. by Y); R12 = as R11 but not H; Y = CF3, CN, F, Cl, Br, I or 1-6C alkyl; Y' = as for Y or SR8, SOR8 or SO2 R8; provided that if Q = OR, R1 = OMe and R2-R6 = H, then R7 is other than Cl.

USE - (I) are cyclooxygenase (COX) inhibitors which selectively inhibit COX-2 in preference to COX-1, and are used for treating COX-mediated and inflammatory disease (all claimed). They may be used for treating inflammatory diseases susceptible to treatment with NSAID's , specifically in patients in which NSAID's are contraindicated (claimed). As selective **COX-2 inhibitors**, (I) have similar antiinflammatory, analgesic and antipyretic activity to conventional NSAID's, and additionally inhibit hormone-induced uterine contractions, have potential anticancer effects, inhibit bone resorption (useful in the treatment of osteoporosis) and are useful in treatment of Alzheimer's disease. Typically (I) are used for: (i) relief of pain, fever and inflammation, e.g. associated with rheumatic fever, influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, degenerative joint diseases, osteoarthritis, gout, ankylosing spondylitis, bursitis, burns, injuries or dental or surgical procedures; (ii) inhibiting prostanoid-induced smooth muscle contractions, e.g. in treatment of dysmenorrhoea, premature labour, asthma and eosinophil related disorders; (iii) inhibiting neoplastic transformations and metastatic tumour growth in the treatment of **cancer**; and (iv) treating COX-mediated proliferative disorders such as diabetic retinopathy and tumour **angiogenesis**.

ADVANTAGE - (I) have reduced side-effects compared with conventional NSAID's, especially reduced potential for gastrointestinal toxicity or renal side-effects, reduced effect on bleeding times and possibly lessened ability to induce asthma attacks in aspirin-sensitive asthmatic patients. Dwg.0/0

ABEQ US 5604253 A UPAB: 19970326
A compound of formula (I) or a pharmaceutically acceptable salt thereof, where Q is (a) -OR or (b) -NR9R10; R is (a) -H or (b) -C1-4 alkyl; R1 is (a) -OCH3, (b) -OCH2F, (c) -OCHF2, (d) F, Cl, Br or I, or (e) methyl or ethyl; R2, R3, R4 and R5 are (a) H, (b) F, (c) methyl or ethyl, (d) -CF3, CF2H, or CFH2, (e) -OH, OR8, SR8, S(O)R8, or S(O)2R8, (f) mono- or di-substituted benzyl, wherein the substituent is (1) H, (2) CF3, (3) CN, (4) F, Cl, Br or I, (5) C1-6alkyl, (6) SR8, S(O)R8, or S(O)2R8, (g) naphthylmethyl, or R2 together with R3 form an oxo group; or R4 together with R5 form an oxo group; or R2 and R3, or R2 and R4, or R2 and R5, or R3 and R4, or R3 and R5, or R4 and R5 are joined so that together with the

carbon atom to which they are attached there is formed a saturated monocyclic hydrocarbon ring of 3, 4, 5, 6 or 7 members; R6 is H or F; R7 is (a) Br, Cl or I, (b) SMe, SEt, or SCF2H; R8 is methyl, ethyl or mono- or di-substituted benzyl, wherein the substituent is (1) H, (2) CF3, (3) CN, (4) F, Cl, Br or I, (5) C1-6alkyl; R9 and R10 are independently (a) H, (b) -C1-3 alkyl, (c) -OR, (d) -C(O)R11, (e) -S(O)2R12, (f) mono-substituted C2-4 alkyl wherein the substituent is selected from (1) hydroxy, (2) amino, (3) methylamino, and (4) dimethylamino, provided that said substituent is located on a carbon of C2-4 alkyl other than the one attached to the nitrogen of -NR9R10, (g) phenyl, benzyl or pyridyl optionally mono- or di-substituted, the substituents are (1) hydrogen, (2) CF3, (3) CN, (4) F, Cl, Br or I, (5) C1-6alkyl; or R9 and R10 are joined so that together with the nitrogen atom to which they are attached there is formed a saturated or unsaturated monocyclic ring of 3, 4, 5, 6, or 7 members, optionally containing one or two additional heteroatoms, said heteroatoms independently selected from N, O and S, said ring optionally containing one or two carbonyl or sulfonyl groups;

R11 is (a) H, (b) C1-4 alkyl, (c) CF3, (d) phenyl or benzyl optionally mono- or di-substituted, the substituents are (1) hydrogen, (2) CF3, (3) CN, (4) F, Cl, Br or I, (5) C1-6alkyl; R12 is (a) -C1-4 alkyl, (b) -CF3, (c) phenyl or benzyl optionally mono- or di-substituted, the substituents are (1) hydrogen, (2) CF3, (3) CN, (4) F, Cl, Br or I, (5) C1-6alkyl;

with the proviso that when Q is OR and R1 is OMe and R2, R3, R4, R5 and R6 are simultaneously hydrogen, R7 is other than Cl.

Dwg.0/0

L11 ANSWER 45 OF 48 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:40954 BIOSIS
DN PREV200000040954
TI Cyclooxygenase-2: A new therapeutic target.
AU Sengupta, S. [Reprint author]
CS Department of Pharmacology, University of Cambridge, Cambridge, UK
SO Indian Journal of Pharmacology, (Oct., 1999) Vol. 31, No. 5, pp. 322-332. print.
CODEN: INJPD2. ISSN: 0253-7613.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 19 Jan 2000
Last Updated on STN: 31 Dec 2001
AB Cyclooxygenase (COX) is the enzyme catalysing oxidation of arachidonic acid to hydroperoxy endoperoxide (PGG2) and its subsequent reduction to hydroxy endoperoxide (PGH2). It is thus an important therapeutic target for the modulation of the prostaglandin pathway. Recent studies have demonstrated the existence of a second isoform of COX. Both the isoforms have a molecular weight of 71K with 63% amino acid homology. The human COX-2 gene is however a 8.3Kb small immediate early gene and is induced by most of the stimuli associated with inflammation. COX-2 has thus been implicated in pathological roles of COX while constitutive COX-1 is said to be involved in physiological functions. Indeed, COX-2 has now been associated with inflammation, hyperalgesia, **angiogenesis**, neuromodulation, **cancer** and Alzheimer's disease, giving rise to the opportunity of modulating these conditions with selective inhibitors of COX-2. The recent X-ray structural analysis for COX-2 has paved the way for development of a whole new range of agents with selectivity for this isoform, thereby sparing the physiological functions. Here in this review, an attempt has been made to elucidate the role of COX-2 in these conditions and to evaluate the various **COX-2 inhibitors** that are in different stages of development or are presently available. From the present knowledge of COX-1 and COX-2 an effort has been made to reclassify NSAIDs based on the selectivity in inhibiting the isoforms.

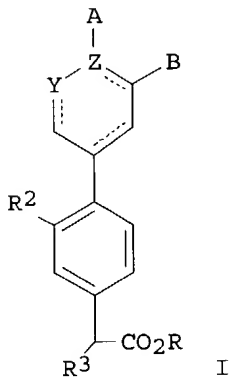
L11 ANSWER 46 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 1999342015 EMBASE
TI Potential utility of **COX-2 inhibitors** in chemoprevention and chemotherapy.
AU Koki A.T.; Leahy K.M.; Masferrer J.L.
CS A.T. Koki, Monsanto Corporate Research, Monsanto-Searle Discovery Research, 700 Chesterfield Parkway North, Chesterfield, MO 63017, United States. ATKOKI@monsanto.com
SO Expert Opinion on Investigational Drugs, (1999) 8/10 (1623-1638).
Refs: 130
ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom
DT Journal; General Review
FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Increased prostaglandin (PG) production is associated with many inflammatory pathophysiological conditions; it is derived from arachidonic acid by either of two enzymes: cyclooxygenase-1 or -2 (COX-1 or COX-2). In addition to its role in inflammation, recent work suggests COX-2 derived prostaglandins may play a pivotal part in the maintenance of tumour viability, growth and metastasis. In this review, we summarise the non-steroidal anti-inflammatory drug (NSAID) epidemiological evidence, studies demonstrating overexpression of COX-2 in multiple human tumours and the pharmacological evidence in animal models which also support this hypothesis. We also discuss the potential functional roles of COX-2 activity during tumourigenesis, and speculate on the mechanism by which **COX-2 inhibitors** may exert their anticancer effects.

L11 ANSWER 47 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:606737 CAPLUS
DN 131:295907
TI Thromboxane A2 is a mediator of cyclooxygenase-2-dependent endothelial migration and **angiogenesis**
AU Daniel, Thomas O.; Liu, Hua; Morrow, Jason D.; Crews, Brenda C.; Marnett, Lawrence J.
CS Departments of Medicine, Cell Biology, Biochemistry, and Pharmacology, Divisions of Nephrology and Hypertension and Clinical Pharmacology, The Vanderbilt Center for Vascular Biology, Vanderbilt Cancer Center, Vanderbilt University, Nashville, TN, 37232, USA
SO Cancer Research (**1999**), 59(18), 4574-4577
CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
AB Cyclooxygenase-2 (**COX-2**) **inhibitors** reduce angiogenic responses to a variety of stimuli, suggesting that products of COX-2 may mediate critical steps. Thromboxane A2 (TXA2) is one of several eicosanoid products generated by activated human microvascular endothelial cells. Selective COX-2 antagonists inhibit TXA2 production, endothelial migration, and fibroblast growth factor-induced corneal **angiogenesis**. Endothelial migration and corneal **angiogenesis** are similarly inhibited by a TXA2 receptor antagonist, SQ29548. A TXA2 agonist, U46619, reconstitutes both migration and **angiogenesis** responses under COX-2-inhibited conditions. These findings identify TXA2 as a COX-2 product that functions as a critical intermediary of **angiogenesis**.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 48 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:529121 CAPLUS
DN 131:157648
TI Preparation of biarylacetic acid derivatives as **COX-2 inhibitors**
IN Bayly, Christopher I.; Black, Cameron; Ouimet, Nathalie; Percival, David; Leger, Serge; Ouellet, Marc
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9941224	A1	19990819	WO 1999-CA120	19990211 <--
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 5994379	A	19991130	US 1999-246925	19990209 <--
	CA 2318966	AA	19990819	CA 1999-2318966	19990211 <--
	AU 9925065	A1	19990830	AU 1999-25065	19990211 <--
	AU 749618	B2	20020627		
	EP 1054857	A1	20001129	EP 1999-904652	19990211
	EP 1054857	B1	20031105		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	JP 2002503647	T2	20020205	JP 2000-531421	19990211
	AT 253545	E	20031115	AT 1999-904652	19990211
PRAI	US 1998-74627P	P	19980213		
	WO 1999-CA120	W	19990211		

OS MARPAT 131:157648
GI



I

AB Title compds. [I; R = H, CH3; R2 = H, F; R3 = H, CH3; Y = C(OEt), C(OMe), N, CH, C:O; Z = C, N; A = H; B = OEt, SEt, OPr, (E)-CH:CHCH3, CH3; A-B = NHC(CH3):CH; CHN(CH3)CH, OC(CH3):CH, SC(CH3):CH, NHC(CH3):N, N:C(CH3)O, N:C(CH3)S, OC(CH3):N, SC(CH3):N, CH2N(CH3)CH, CHC(CH3)N:CH; dotted bond = single, double in relation to Y, Z, A, B], pharmaceutically acceptable salts (sodium, potassium, calcium, magnesium), tautomer, and esters

thereof are prepared and compns. which contain such compds. and methods of use the compds. are presented and tested as inhibitors of COX-2. Thus, the title compound I (Y = C(OEt); Z = C; A = H; B = OEt; R = H; R2 = H; R3 = CH3; dotted bonds = double bonds) was prepared from 3,5-diethoxyphenol in 3 steps.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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